

### ***Remarks***

#### ***Status of the Claims and Support for the Amendments***

By the foregoing amendments, claims 35-186, 220-222 and 226-227 have been canceled without prejudice or disclaimer. Applicants reserve the right to prosecute the subject matter of these claims in one or more divisional or continuation applications. New claims 228-248 are sought to be added. Support for new claims 228-248 can be found throughout the present specification, specifically throughout pages 18-31 and the Examples. Upon entry of the foregoing amendments, claims 187-219, 223-225 and 228-248 are pending in the application, with claims 187, 213 and 228 being the independent claims. Claims 213-219 and 223-225 have been allowed.

#### ***Summary of the Office Action***

In the Office Action dated May 26, 2005, the Examiner has made one objection to, and five rejections of, the claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

#### ***The Rejections Under 35 U.S.C. § 112, Second paragraph***

In the Office Action at pages 3-4, section 1, the Examiner has maintained the rejection of claims 57-58, 96-97, 132-133 and 196-197 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. By the foregoing amendments, claims 57-58, 96-97 and 132-133 have been canceled. Hence, this rejection

has been rendered moot with respect to these claims. Applicants respectfully traverse this rejection as it may apply to claims 196 and 197.

The Examiner contends that the phrase "immediately adjacent " is not defined in the specification and that it is unclear what the structural/functional requirements are for satisfying this limitation. The Examiner also contends that the term is not clearly defined in the art and is therefore subjective. Applicants respectfully disagree with these contentions. Applicants incorporate by reference herein the remarks made in their reply dated March 22, 2005. In addition, Applicants submit the following additional remarks.

Applicants respectfully submit that the ordinarily skilled artisan, guided by the present specification, would clearly understand the metes and bounds of the term "immediately adjacent," as that term is used in the presently claimed invention. The Examiner's attention is directed to Figure 4C of the present application. Applicants submit that Figure 4C clearly depicts an SP6 promoter located "immediately adjacent" to a *loxP* site. The ordinarily skilled artisan would readily understand that the orientation depicted in this figure represents a site-specific recombination site "immediately adjacent" to a promoter. Applicants further submit that the term "immediately adjacent" would be readily understood to mean that there are no intervening nucleotides between the two structures.

Figure 4C does not simply show one structure *next to* another structure, as the Examiner has indicated in the Office Action at page 6, lines 3-4 with regard to similar figures 8B, 8I and 8J (which Applicants submit also represent structures that are "immediately adjacent" to one another). Rather, Figure 4C depicts an SP6 promoter *immediately adjacent to a loxP site-specific recombination site*, where there are no

intervening nucleotides between the two structures. The ordinarily skilled artisan, guided by the present specification, and specifically Figure 4C, would readily understand that the SP6 is "immediately adjacent" to the *loxP* site, with no intervening nucleotides, and not simply "next to" the *loxP* site.

Applicants respectfully note that the Examiner's interpretation of a claim term must be consistent with that interpretation those skilled in the art would reach. *See In re Cortright*, 165 F.3d 1353 (Fed. Cir. 1999); *see also* M.P.E.P. § 2111 at 2100-47. Simply interpreting Figure 4C to mean that the SP6 promoter and the *loxP* site are "next to" one another would be contrary to the purpose of the figure, which is to provide the ordinarily skilled with a detailed diagram of the spatial orientation of the various components of plasmid pEZC1003. The ordinarily skilled artisan would readily understand the detail provided in Figure 4C and would not consider the SP6 promoter to simply be "next to" the *loxP* site, but rather, would understand that these two structures are "immediately adjacent to" one another, with no intervening nucleotides, as shown in the figure.

To provide further support for this interpretation, the Examiner is directed to page 38, lines 1-15 of the present specification. The schematic at lines 4-10, reproduced below, represents the nucleotide regions that participate in an *att* recombination reaction in *E. coli*.

attP--P1--H1--P2--X--H2--C-O-C'--H'--P'1--P'2--P'3--

+

attB --B-O-B'--

Int, IHF ↓ Xis, Int, IHF

attR --P1--H1--P2--X--H2--C-O-B'--

+

attL --B-O-C'--H'--P'1--P'2--P'3--

In describing this schematic, the present specification states that "O represents the 15 bp core DNA sequence found in both the phage and *E. coli* genomes; B and B' represent approximately 5 bases *adjacent* to the core in the *E. coli* genome;" (Specification at page 38, lines 11-13, emphasis added). Applicants respectfully submit that the ordinarily skilled artisan would readily understand, as stated, that B and B' are "adjacent" to the 15 bp core region "O," and as illustrated, have no intervening nucleotides between the core region, "O," and the 5 base pair B and B' regions (*i.e.*, no additional nucleic acids are shown in the schematic). The term "immediately" was added to the present claims to further clarify that two structures that are "adjacent" or "immediately adjacent" to one another are not simply "next to" one another, but rather are separated by no intervening nucleotides, as shown in the schematic above, and in Figure 4C as discussed above (as well as in Figures 8B, 8I and 8J).

In view of the foregoing remarks, Applicants respectfully submit that there is sufficient literal support for the phrase "immediately adjacent" in the present specification such that the ordinarily skilled artisan would readily understand the metes and bounds of this

phrase as it is used in the present claims. Hence, Applicants submit that this term is not indefinite, and that the present claims do comply with the requirements of 35 U.S.C § 112, second paragraph. Therefore, reconsideration and withdrawal of the rejection of claims 196 and 197 are respectfully requested.

***The Rejections Under 35 U.S.C. § 112, First paragraph***

In the Office Action at pages 5-6, section 2, the Examiner has maintained the rejection of claims 57-58, 96-97, 132-133 and 196-197 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. By the foregoing amendments, claims 57-58, 96-97 and 132-133 have been canceled. Hence, this rejection has been rendered moot with respect to these claims. Applicants respectfully traverse this rejection as it may apply to claims 196 and 197.

The Examiner contends that there is no literal support for the phrase "immediately adjacent to" recited in the present claims. Applicants respectfully disagree with this contention.

As discussed above, and in their previous reply, Applicants submit that the term "immediately adjacent" would be readily understood by the ordinarily skilled artisan to mean that the recombination sites and the related genes, portions of genes, etc., have no intervening nucleotides between them. Contrary to the Examiner's assertion, Applicants respectfully submit that the ordinarily skilled artisan, guided by the present specification and figures, would understand that the term "immediately adjacent" does not simply mean that

two structures are next to each other, but rather, that two structures have no intervening nucleotides between them.

With regard to the Examiner's statement that " the cited figures are ambiguous as to whether 'immediately adjacent' encompasses a genus of sequences with a particular structural limitation," (Office Action at page 6, second paragraph, lines 4-6), Applicants respectfully submit that the ordinarily skilled artisan would readily understand that the phrase "immediately adjacent" clearly does encompass a genus of sequences with the particular structural limitation of having two structures (e.g., a recombination site and a promoter) together with no intervening nucleotides between them.

In view of the foregoing remarks, Applicants respectfully submit that there is sufficient literal support for the phrase "immediately adjacent" in the present specification such that the ordinarily skilled artisan would readily understand this phrase as it is used in the present claims. Hence, Applicants submit that this term is not new matter, and that the present claims do comply with the written description requirement of 35 U.S.C § 112, first paragraph. Therefore, reconsideration and withdrawal of the rejection of claims 196 and 197 are respectfully requested.

***The Rejection Under 35 U.S.C. § 102(b) Over Johnson***

In the Office Action at pages 6-11, section 3, the Examiner has maintained the rejection of claims 35-71, 74-77, 158-180 and 183-186 under 35 U.S.C. § 102(b), as allegedly being anticipated by Johnson *et al.* WO 93/19172 (hereinafter "Johnson"). Applicants respectfully traverse this rejection. However, solely to expedite prosecution, and

not in acquiescence to this rejection, claims 35-71, 74-77, 158-180 and 183-186 have been canceled. Hence, this rejection has been rendered moot.

***The Rejection Under 35 U.S.C. § 102(b) Over Fukushima***

In the Office Action at pages 11-12, section 4 the Examiner has rejected claims 78, 81-85, 96-100, 102-108, 115, 118-121, 132-136, 138-141 and 151 under 35 U.S.C. § 102(b), as being allegedly anticipated by Fukushima *et al.*, *Proc. Natl. Acad. Sci.* 89: 7905-7909 (1992) (hereinafter "Fukushima"). Applicants respectfully traverse this rejection. However, solely to expedite prosecution, and not in acquiescence to this rejection, claims 78, 81-85, 96-100, 102-108, 115, 118-121, 132-136, 138-141 and 151 have been canceled. Hence, this rejection has been rendered moot.

***The Rejection Under 35 U.S.C. § 103(a) Over Fukushima, In View of Johnson and Lenski***

In the Office Action at pages 13-16, section 5, the Examiner has rejected claims 78-87, 96-111, 115-123, 132-141 and 151-153 under 35 U.S.C. § 103(a), as allegedly being unpatentable over Fukushima, in view of Johnson and further in view of Lenski *et al.*, *J. Bact.* 176:3140-3147 (1994) (hereinafter "Lenski"). Applicants respectfully traverse this rejection. However, solely to expedite prosecution, and not in acquiescence to this rejection, claims 78-87, 96-111, 115-123, 132-141 and 151-153 have been canceled. Hence, this rejection has been rendered moot.

***The Objection to Claims 154-157***

In the Office Action at page 2, the Examiner has objected to claims 154-157. By the foregoing amendments, claims 154-157 have been canceled. Hence, this objection has been rendered moot.

***The Rejection of Claims 187-195 and 198-212***

Applicants note that on the Office Action Summary form, as well in the Conclusion of the Office Action at page 16, the Examiner has indicated that claims 187-195 and 198-212 have been rejected. However, Applicants note that in the body of the Office Action, the Examiner has not set forth any grounds of rejection or objection with regard to these claims.

Applicants respectfully remind the Examiner that for a rejection of one or more claims to be proper, the *reasons* for the rejection must be clearly stated in the Office Action. *See* 37 C.F.R. § 1.104(a)(2). Since the reasons for any alleged rejection of claims 187-195 and 198-212 have not been stated in the present Office Action, Applicants presume that the inclusion of these claims in the list of rejected claims was in error. Applicants therefore respectfully submit that claims 187-195 and 198-212 (as well as claims 196-197 as discussed above) are allowable, along with claims 213-219 and 223-225, which have been as indicated as allowable by the Examiner.

In addition, Applicants submit that new claims 228-238, drafted so as to mirror allowed claims 213-219 and 223-225, are also allowable. Finally, Applicants respectfully submit that new claims 239-248, which depend ultimately from independent claim 187, are also allowable.



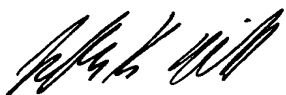
***Conclusion***

All of the stated grounds of rejection and objection have been properly traversed, rendered moot or otherwise overcome. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and objections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Jeffrey K. Mills  
Agent for Applicants  
Registration No. 56,413

Date: August 23, 2005

1100 New York Avenue, N.W.  
Washington, D.C. 20005-3934  
(202) 371-2600